Symposium Section

The Plasma Bank

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UNTIL relatively recently the terms "blood bank" and "plasma bank" would have baffled the most learned lexicographer. Their current wide adoption even by laymen not only implies their ready acceptance and thorough comprehension but also indicates the intensive development of this subject within a few years. The terms are not merely metaphoric, but essentially descriptive. The basic principles of the operation of a blood or plasma bank are similar to those of a business bank. One cannot withdraw money from a bank without having previously made a sufficient deposit or borrow money without having made provisions for repayment. Similarly in a blood bank the deposition of blood must precede withdrawal and a loan must be repaid, for obviously depletion without replenishment would soon cause bankruptcy or cessation of the blood bank's function.

Whereas the idea of a blood or plasma bank is not new, its practical realization is relatively recent. Over 70 years ago various investigators were studying the value of plasma and serum in perfusion experiments. Indeed the procedure of transfusion of stored blood was suggested as early as 1875 by Freer. This investigator, on the basis of experimental investigations in which dogs were transfused with blood that had been preserved in the refrigerator for 72 hours, stated that: "The practical value of a knowledge of these facts we believe to be of great importance, in relation to the operation of blood transfusion, for this knowledge removed apprehension concerning the integrity of the blood, when transfusing, leisurely, which is essential to successful avoidance of distressing, if not dangerous, symptoms; also it renders it possible to save up blood for future use, the convenience of which must be apparent—." In 1907, Gutherie and Pike showed experimentally that plasma and serum were effective in the treatment of hemorrhage and subsequently a number of investigators confirmed these observations. In 1914, Abel and his co-workers envisioned the possibilities of the storage of blood for emergency use. During the last Great War, Ward, recognizing the difficulties of whole blood transfusion in emergencies, suggested the use of plasma. Similarly Rous and Wilson directed attention to the advantages of plasma in such cases. In 1916, Rous and Turner demonstrated the practicability of transfusing conserved blood and two years later Robertson published an account of its application in the United States Army Medical Service. However, for some curious reason, these promising developments lagged for over a decade and then, with the presentation by the Russian workers of their investigations on stored blood and cadaver blood transfusion, fresh impetus was given to the study. In this country probably the first "blood bank" was developed at Cook County Hospital. Since then extensive experimental and clinical investigations have been reported, clearly establishing the practical value of stored blood and plasma in the treatment of hemorrhage, shock, burns and hypoproteinemia.

As previously emphasized, there are a number of practical advantages to the use of blood plasma over whole blood. In transfusing whole blood it is necessary to obtain a suitable donor, which requires compatibility and serologic tests. These are time-consuming procedures which in emergencies may be significant. Moreover, the availability of donors is an important factor to consider, especially in military practice in which therapeutic measures must be instituted under adverse circum-

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stances and in which expediency is an absolute necessity. These difficulties can be readily obviated by the use of plasma. By adequate preparation, large quantities of plasma may be provided in advance and safely stored for long periods without deterioration and be ready for instant use. Preliminary typing and compatibility tests are unnecessary because iso-agglutinins are partially suppressed by pooling and further inhibited by the patient's blood. Plasma can also be readily transported by various means of conveyance without the inconvenience of refrigeration and administered with the simplicity and facility of ordinary saline solution.

Aside from these technical advantages, extensive clinical and experimental investigations have clearly demonstrated that plasma is not only a satisfactory substitute for whole blood in the treatment of most conditions, but in some cases is distinctly superior. It is now well established that diminished circulating blood volume is one of the most significant features in peripheral circulatory failure or shock due to hemorrhage, trauma, or burns. In hematogenic shock the decrease in circulating blood volume is due to the loss of whole blood but in other types of shock, such as "wound shock" or that consequent to trauma and burns, it is due primarily to loss of blood plasma. Accordingly, the rational treatment of such conditions is based upon an attempt to produce a prompt return to normal of the circulating blood volume and to maintain it at this level. The most effective means of accomplishing this is by the intravenous administration of a fluid similar in constituency to blood. This is due to the fact that in such states as described above there is a depletion of plasma proteins which are essential in maintaining osmotic pressure and therefore in holding fluids in the vascular tree and attracting them from the tissues. Accordingly, the addition of noncolloidal solutions, such as isotonic salt solution or glucose solution, merely dilutes the plasma proteins, with consequent diminution of the osmotic pressure, resulting in a greater and more rapid escape of fluid from the vessels which is further enhanced by the increased permeability due to capillary damage by anoxia. Thus, it becomes obvious that no other substance can act as efficaciously as blood in substantially increasing and maintaining circulating blood volume in the presence of a previously depleted vascular system. Because of certain inherent disadvantages in the use of whole blood, various attempts have been made to use a substitute fluid more readily available. With the exception of plasma or serum which, strictly speaking, cannot be considered substitute fluids because they contain practically all the fluid elements of whole blood, none of the substitutes has proved wholly satisfactory.

As previously stated, in many conditions plasma is not only just as effective therapeutically as whole blood but in some is even more rational. Thus, in peripheral circulatory failure due to local trauma or visceral exposure and in burns, there is "plasma loss" and usually hemoconcentration. In such states the diminution in blood volume is more effectively corrected by the transfusion of plasma rather than whole blood, because the addition of red blood cells is not only unnecessary, but theoretically might be harmful. On the other hand, because in severe hemorrhage the cellular as well as the fluid element is lost, the transfusion of whole blood would appear more rational. Under such circumstances, the loss of red blood cells may embarrass the oxygen-carrying capacity of the circulating blood. Accordingly, the transfusion of whole blood not only supplements the circulating blood volume but replenishes its oxygen-carrying capacity. While this is undoubtedly true, it should be realized that even in hematogenic shock the transfusion of plasma is also beneficial and effective because in such a condition the most pressing need is the restoration of circulating blood volume.

Increase in circulating blood is not the only rationale for plasma transfusion. As previously emphasized, blood transfusion may be considered essentially as replacement therapy and in this respect plasma is just as efficacious as whole blood in most conditions. Perhaps the most prominent exceptions to this are those states requiring increase in oxygen-carrying capacity. Thus, whole blood is preferable in severe hemorrhage or in pronounced acute and chronic anemias, in certain forms of intoxications and poisonings such as carbon

monoxide and nitrobenzol poisoning, in which the hemoglobin combines with the poison to form a stable compound and thus loses its oxygen-carrying capacity, and in certain forms of leukopenia or agranulocytosis. On the other hand, plasma is preferable in shock not due to hemorrhage, in burns, in nutritional edema associated with hypoproteinemia but not anemia, in nephritis with edema, in nephrosis, and concentrated plasma in cerebral edema. In most infections fresh whole blood is probably preferable, although in certain forms of infections not associated with anemia properly prepared plasma may be just as satisfactory. It is considered inexpedient to attempt here a detailed account of the various advantages and indications of plasma and whole blood, respectively, as such considerations may be found elsewhere. According to Strumia and McGraw, they may be summarized as follows:

1. Shock:
   (*a*) Associated with little or no hemorrhage —Plasma.
   (*b*) With severe hemorrhage—Plasma for immediate relief, followed by whole blood if warranted.
2. Burns:
   Plasma. (It should be added that in late burns accompanied by anemia whole blood is indicated.)
3. Infections:
   (*a*) For the purpose of supplying specific and nonspecific immune bodies—Plasma.
   (*b*) Supplement with whole blood in presence of severe anemia.
4. Hypoproteinemias:
   Due to nutritional, hepatic, nephrotic, and other causes—Plasma.
5. Cerebral edema:
   Due to injuries, toxemias, etc.—Plasma.
6. Blood dyscrasias:
   (*a*) Those with hemolytic tendencies, low prothrombin content, hemophilia, etc.—Plasma.
   (*b*) Those with hemorrhagic tendencies as in certain forms of purpura—Whole blood.
7. Anemias:
   As palliative procedure in various hypoplastic forms—Whole blood; plasma in chronic forms of hypoproteinemic anemias.
8. Acute poisonings:
   Affecting the oxygen-carrying capacity of hemoglobin, such as carbon monoxide poisoning—Whole blood.

Various methods have been proposed in the preparation and preservation of plasma. In general they may be classified into two types: (1) those directed toward preparing and preserving fresh liquid plasma; and (2) those directed toward preparing dried plasma. It is inopportune to attempt here a detailed discussion of the advantages and disadvantages of these various methods. This phase of the subject has been adequately reviewed in a previous publication. Strumia and McGraw have recently considered the best methods of preparing and preserving plasma and have directed attention to certain significant observations. One of the most common methods of preserving plasma in the liquid state consists essentially in keeping it in the refrigerator at a temperature of +4° to +6° C. It was soon found that there were certain objections and even dangers associated with this method. Because it is accompanied by progressive flocculation of the most unstable proteins, it requires filtration previous to administration. The use of such plasma without previous filtration has caused at least one reported death. Bacterial contamination and the development of pyrogenic substances is another danger associated with this method of preserving liquid plasma. Strumia and McGraw emphasize the importance of not relying too much upon the addition of bacteriostatic substances such as merthiolate. They recently reported five severe reactions following the administration of such plasma. Still another important objection to this method of plasma preservation is the continuous and progressive loss of such essential elements as prothrombin and complement. For these reasons this method of preparing and preserving plasma is considered undesirable.

On the basis of their extensive investigations Strumia and McGraw have come to the conclusion that the preservation and storage of plasma in the frozen state is the method of choice. The advantages of this method consist essentially in ease of preparation, economy, ease of storage and of transportation, retention of the most labile elements such as prothrombin and complement, maintenance of sterility, elimination of flocculation and consequent filtration before administration, and in not requiring water for restoration in contradistinc-

tion to dried plasma. Another advantage of this method is that dried plasma, which has certain advantages especially in military practice, is best prepared from the frozen state.

In order to assure these advantages in the application of this method of plasma preservation, Strumia and McGraw have emphasized certain essential technical considerations to which strict adherence is necessary. These consist briefly in freezing the plasma fairly rapidly, *i.e.*, within three to six hours; maintaining the frozen plasma in storage at a definitely safe level below freezing, -10° C. or below; and thawing rapidly and warming to room temperature in a water bath at +37° C. with occasional gentle agitation, the procedure not requiring more than 25 minutes.

For the reasons stated above only the method described by Strumia and McGraw will be considered here. This method of plasma preparation may be divided into several parts: (1) collection of blood; (2) separation, pooling, and distribution of plasma; (3) freezing and preservation of plasma. It should be realized that this is essentially a closed system, permitting minimal transfers and manipulations. Strict adherence to an aseptic technique is further necessary to maintain sterility.

In the collection of blood certain apparatus is necessary. This has been described in detail and illustrated in previous publications, and consists essentially of an 850-cc. pyrex bottle having a short neck fitted with a hooded rubber stopper provided with two holes into each of which is inserted a glass tube (Figs. 1*a* and 1*b*). One of these glass tubes is connected by a small length of rubber tubing to a mouthpiece with a saliva trap (Fig. 1*c*) and the other by longer tubing to a glass needle adapter which is protected by inserting it in a small test tube (Fig. 1*d*). The donor needle is prepared by placing it in an hourglass container stoppered with cotton (Fig. 1*e*). After assembling these various parts and placing 50 cc. of 4 per cent sodium citrate in normal saline solution in the bottle, the entire apparatus is sterilized in the autoclave. The apparatus is now ready for the collection of blood from the donor.

In the selection of a prospective donor, certain considerations such as age, general health, and freedom from communicable disease are important. While the drinking of several glasses of a nonfatty fluid is encouraged, the donor should avoid a meal during the four hours preceding the bleeding. After selecting a suitable vein, the area is adequately prepared and draped as in the preparation of an operative field. Since strict asepsis is necessary, the operator should also prepare himself as for a surgical operation. The site and technical considerations of venipuncture have been previously described and illustrated in detail. After applying the donor needle to the needle adapter, the venipuncture is performed and by applying suction to the mouthpiece a continuous flow into the bottle is assured. The bottle should be gently rotated to insure adequate mixture with the anticoagulant. After collecting the full amount (3 cc. per pound of body weight for females and 3.5 cc. per pound for males) the tourniquet is released, the donor tube is pinched, and the needle removed from the vein. The glass adapter from which the donor needle has been removed is then placed in the glass test tube. By milking the rubber tube, the blood remaining in it may be discharged into the glass tube for subsequent serologic tests. The two rubber tubes are then slightly pulled and folded down alongside the neck of the bottle and fixed tightly with stout rubber bands, thus effectively sealing the bottle. Two identification tags, one for the collecting bottle and the other for the glass tube containing the blood for typing and serologic tests, are filled out. The bottle containing blood withdrawn from the donor should be placed in the refrigerator at 4° C. as soon as possible after collection and kept there until used or the plasma is separated.

Obviously this method is readily applicable to the purpose of a blood bank. If a whole blood transfusion is desired the procedure consists essentially of removing the hooded rubber stopper and applying another provided with a setup for dispensing the blood and consisting essentially of a rubber stopper having two holes, into one of which is fitted a long glass tube to act as an air vent and another shorter tube which is connected to a length of tubing having a recipient's needle at the end. If the blood is to be used for the

preparation of plasma, it is extremely desirable to diminish as much as possible the time interval between the collection of blood and the separation and "fixation," *i.e.*, the freezing, of plasma. The importance of this lies in the fact that possible bacterial growth from even minor contamination is minimized and greater retention of the most labile elements such as prothrombin and complement is assured. In any case it is desirable to store whole citrated blood not longer than 3 to 5 days before separation of plasma.

Separation of plasma is effected by centrifugation or sedimentation. The former is the procedure of choice because it permits a higher yield and the procurement of fresh plasma which is distinctly superior. The special centrifuge preferred by Strumia and McGraw is the No. 3 International Centrifuge Model F. S. capable of maximal speed of 2500 r.p.m. and provided with a speed regulator and tachometer. Careful attention to the details of centrifugation is important; these have been described in previous publications.

After centrifugation it becomes necessary to draw off, pool and distribute the plasma. The value of pooling lies in the fact that a more uniform product may be obtained, dilution of occasional high agglutinin titer is permitted, and bacteriologic control study is simplified. In order to minimize bacterial contamination during this process, it is essential that an absolutely closed system be employed. For practical purposes the size of the pool

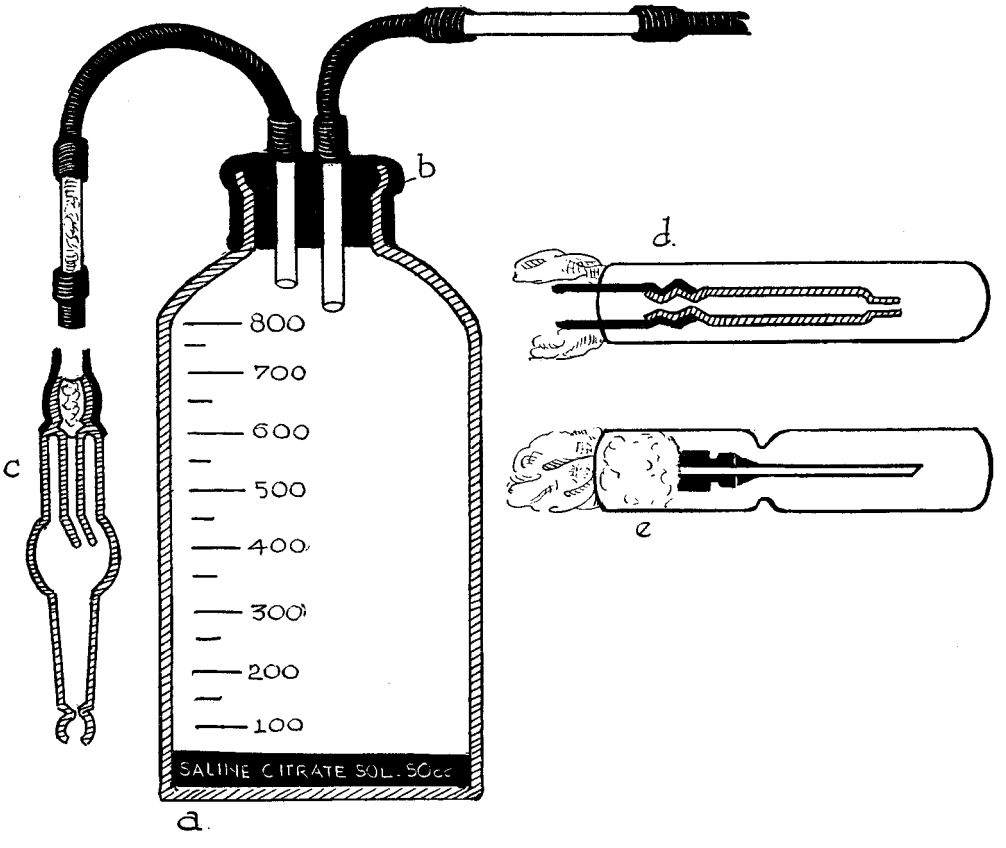

Figure 1.—Component parts of blood-taking bottle as advocated by Strumia and McGraw. (*a*) Pyrex bottle containing citrate saline solution and provided with (*b*) hooded rubber stopper having two holes fitted with glass tubes, one of which is connected by length of rubber tubing to (*c*) mouthpiece with saliva trap, and the other to (*d*) a glass needle adapter fitted with a protecting glass test tube to which may be attached (*e*) the donor needle.

must be limited and in the experience of Strumia and McGraw it is satisfactory to pool 10 individual bleedings averaging 300 cc. each.

The apparatus required for this procedure consists of a 4-liter pooling bottle provided with a two-holed rubber stopper into each of which is fitted a glass tube (Figs. 2*a* and 2*b*). One of these glass tubes, which is partially closed at each end and filled with cotton to form an air filter (Fig. 2*c*), is connected to a vacuum pump when plasma is drawn into the bottle and to a pressure pump when plasma is being distributed in individual containers. The other tube (Fig. 2*d*) is connected on the inside of the bottle to a longer tube which reaches to the bottom of the bottle and on the outside of the bottle to a T tube (Fig. 2*e*), one arm of which leads to an aspirating cannula for drawing the plasma (Figs. 2*f* and 2*g*), and the other to the distributing burette (Figs. 2*h* and 2*i*) for distributing the

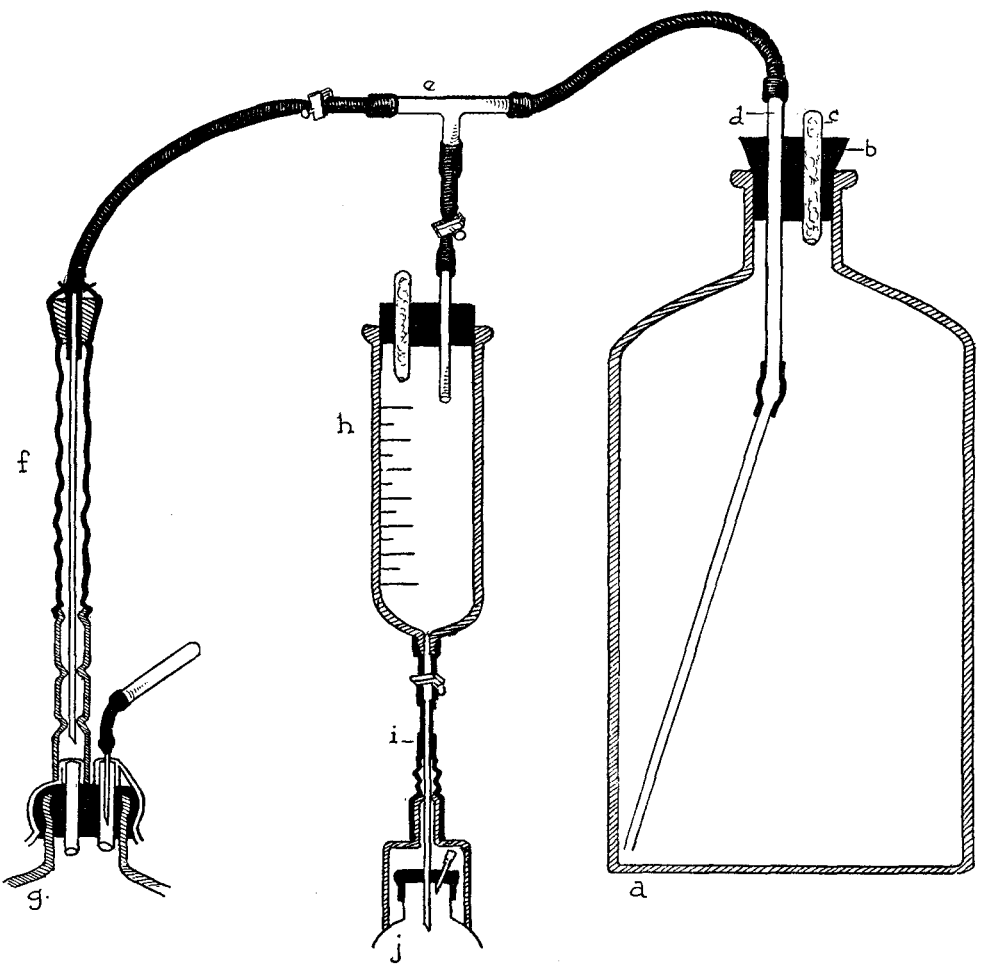

Figure 2.—Closed system apparatus for drawing, pooling, and distribution of plasma as advocated by Strumia and McGraw. (*a*) The 4-liter pooling bottle is fitted with (*b*) a rubber stopper having two holes one of which contains (*c*) an air filter glass tube and the other (*d*) another glass tube which is connected on the inside of the bottle to a longer tube reaching to the bottom of the bottle, and on the outside to (*e*) a T tube, one arm of which leads to (*f*) an aspirating cannula for drawing the plasma from (*g*) the collecting bottle, and the other to (*h*) a distributing burette which is connected at the bottom to (*i*) a specially constructed rubber and glass hooded cannula for distributing the plasma to (*j*) the final containers.

plasma to the individual containers (Fig. *2j*). The cannula used for aspirating the plasma from the collecting bottles and that used for distributing the plasma to the individual containers are protected by specially constructed rubber sleeves and glass hoods, the details of which are illustrated in Figures *2f* and *2i*. After this apparatus is properly assembled, the screw-clamps on the tube leading to the distributing burette and on that leading to the aspirating cannula are closed and vacuum created in the pooling bottle by applying suction. The aspirating cannula (Fig. *2f*) is then inserted through the rubber tube and pulled taut to form a diaphragm over the opening of the glass tube in the collecting bottle (Fig. *2g*) until it reaches the plasma. An air vent is pushed through the diaphragm of the other tube to permit replacement by air of the plasma drawn off. The screw-clamp on the tube leading from the aspirating cannula is then released, allowing plasma to be drawn into the pooling bottle. Aspiration is continued until only a thin layer remains. The aspirating cannula is then removed and the procedure repeated with the next bottle until the desired number of plasmas, approximately 10, have been pooled. The screw-clamp on the tube leading from the aspirating cannula is then closed and the plasma in the pooling bottle is mixed by gentle rotation. A specimen of the pooled plasma may be obtained for bacteriologic study or other examinations by applying air pressure to the pooling bottle, inserting the specially constructed distributing cannula through a perforable rubber stopper of a culture medium bottle and releasing the screw-clamp on the tube leading to the distributing burette. Before distributing the plasma, 0.1 cc. of 10 per cent merthiolate solution for every 100 cc. of plasma is added by aspirating the prepared amount into the pooling bottle in a manner similar to that used for aspirating the plasma from the collecting bottle. The plasma may then be distributed to the individual containers by closing the screw-clamp on the tube leading to the aspirating cannula and that on the tube leading from the distributing burette to the distributing cannula, opening the screw-clamp leading to the distributing burette, and applying air pressure to the pooling bottle. As the plasma enters the burette, the air is displaced through the filter tube in the stopper and when the desired amount of plasma is obtained the clamp on the tube leading to the burette is tightened. The specially constructed cannula leading from the burette (Fig. *2i*) is inserted through the rubber stopper of the final container (Fig. *2j*) and the plasma in the burette allowed to enter it by opening the clamp on the rubber tube leading from the burette. It should be observed that a sterile hypodermic needle is inserted through the rubber stopper of the final container to act as an air vent while the plasma is being introduced. Both the distributing cannula and hypodermic needles are removed from the stopper of the final container after all the plasma in the burette has entered the final container and the clamp on the tube leading from the burette is tightened. This procedure is repeated for each distribution of plasma.

The plasma which is now in the final container is ready for storage. As previously emphasized, it is best preserved in the frozen state and it is important that the "fixation" or freezing be done as soon as possible after the plasma is placed in the final container. The essential technical features of this method of preservation consist of fairly rapid freezing and maintenance at a fairly low temperature, -10° C. or below. Various forms of freezing cabinets, most commonly employed for the storage of ice cream and capable of maintaining temperatures of -15° C. to -20° C., may be obtained for this purpose. The final container of plasma is placed in such a cabinet in a slanting position so as to obtain the largest possible surface of the plasma fluid.

In preparing this frozen plasma for administration certain technical steps must be closely followed. These consist briefly of rapid thawing in a water bath at 37° C. After the container of frozen plasma is removed from the freezing cabinet, it is immediately immersed in a water bath at 37° C. and kept there with occasional gentle rotation and shaking until the plasma has thawed completely, a process usually requiring about 30 minutes. It is then allowed to remain in the water bath for 5 or 10 minutes longer to allow it to reach room temperature. Obviously it is desir-

able to administer the plasma as soon as possible after it has completely thawed. In this clear state it may be safely administered without filtration. If the administration must be delayed for a number of hours, it should be kept at room temperature.

In the administration of this plasma it is desirable to use the same container. This may be accomplished by employing a container having a rubber stopper provided with a long glass tube to act as an air vent and extending from the stopper to within a short distance of the bottom of the bottle. By perforating, with a needle, the thin rubber membrane covering the tube an air vent is created. The bottle is provided with a cloth sling for suspension in the inverted position. The plasma may then be administered by inserting through the rubber stopper a large bore needle which is connected to a length of rubber tubing having a glass adapter at the other end to be fitted to the venipuncture needle.

As previously stated, another advantage of storing plasma in the frozen state is that this is the best method of preparing dried plasma. There are certain distinct advantages and indications for dried plasma, especially in military practice, as demonstrated by the fact that it is the method currently employed by the United States Army and Navy. No attempt will be made here to describe the technique of preparing dried plasma as this has been adequately presented in recent publications.

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